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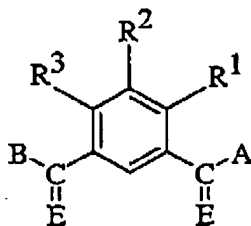
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## AMENDMENT TO THE CLAIMS

The following listing of claim(s) will replace all prior versions, and listings, of claim(s) in the application.

Listing of claim(s):

**Claim 1 (amended).** A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula I



I

wherein:

$R^1$ ,  $R^2$ , and  $R^3$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  $NR^4R^5$ , CN, or  $CF_3$ ;

E is independently O or S;

A and B independently are  $OR^4$  or  $NR^4R^5$ ;

each  $R^4$  and  $R^5$  independently are H,  ~~$C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heterocyclyl,~~  
 $(CH_2)_n$  heteroaryl, or  $R^4$  and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

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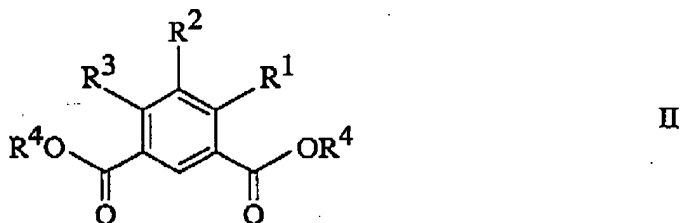
n is an integer from 0 to 6;

or a pharmaceutically acceptable salt thereof;

wherein the compound isophthalic acid bis-(1,3-benzodioxol-5-ylmethyl)  
ester is excluded.

**Claim 2 (amended).**

A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula II



wherein:

R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN, or CF<sub>3</sub>; and

R<sup>4</sup> and R<sup>5</sup> is independently H, ~~C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, (CH<sub>2</sub>)<sub>n</sub> aryl, (CH<sub>2</sub>)<sub>n</sub> cycloalkyl, or (CH<sub>2</sub>)<sub>n</sub> heterocyclyl,~~ (CH<sub>2</sub>)<sub>n</sub> heteroaryl, or R<sup>4</sup> and R<sup>5</sup> when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6;

or a pharmaceutically acceptable salt thereof;

wherein the compound isophthalic acid bis-(1,3-benzodioxol-5-ylmethyl)  
ester is excluded.

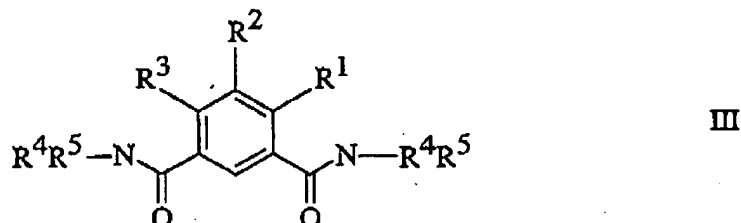
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**Claim 3 (amended).**

A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula III



wherein:

$R^1$ ,  $R^2$ , and  $R^3$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  $NR^4R^5$ , CN, or  $CF_3$ ;

$R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heterocyclyl,  $(CH_2)_n$  heteroaryl, or  $R^4$  and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

$n$  is an integer from 0 to 6;

or a pharmaceutically acceptable salt thereof.

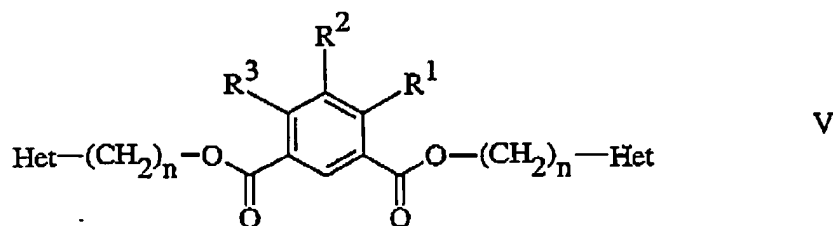
**Claim 4 (canceled).****Claim 5 (amended).**

A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula V

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wherein:

$R^1$ ,  $R^2$ , and  $R^3$  independently are hydrogen, halo, hydroxy,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $NO_2$ ,  $NR^4R^5$ , CN, or  $CF_3$ , and Het is an unsubstituted or substituted heteroaryl group;

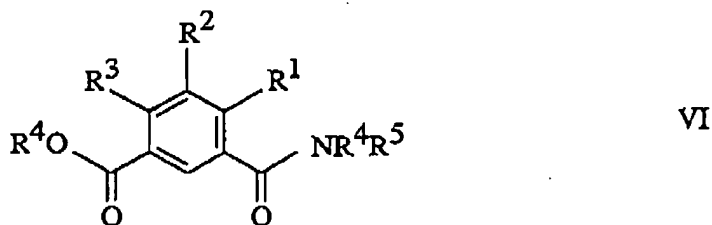
$R^4$  and  $R^5$  independently are H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $(CH_2)_n$  aryl,  $(CH_2)_n$  cycloalkyl,  $(CH_2)_n$  heterocyclyl,  $(CH_2)_n$  heteroaryl, or  $R^4$  and  $R^5$  when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

$n$  is an integer from 0 to 6;

or a pharmaceutically acceptable salt thereof;

wherein the compound isophthalic acid bis-(1,3-benzodioxol-5-ylmethyl) ester is excluded.

**Claim 6 (amended).** A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering to the mammal an MMP inhibiting amount of a compound of Formula VI



or a pharmaceutically acceptable salt thereof,

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wherein:

R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> independently are hydrogen, halo, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, NO<sub>2</sub>, NR<sup>4</sup>R<sup>5</sup>, CN, or CF<sub>3</sub>;

R<sup>4</sup> and R<sup>5</sup> independently are H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, (CH<sub>2</sub>)<sub>n</sub>-aryl, (CH<sub>2</sub>)<sub>n</sub>-cycloalkyl, (CH<sub>2</sub>)<sub>n</sub>-heterocyclyl, (CH<sub>2</sub>)<sub>n</sub>-heteroaryl, or R<sup>4</sup> and R<sup>5</sup> when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted; and n is an integer from 0 to 6.

**Claim 7 (amended).** A compound selected from:

4-Methoxy-N,N'-bis-(4-methoxybenzyl)-isophthalamide;  
 Isophthalic acid di-(2,1,3-benzothiadiazol-5-yl) methyl ester;  
~~4-Methoxy-isophthalic acid dibenzyl ester;~~  
 4-Methoxy-isophthalic acid dipyridin-4-ylmethyl ester;  
~~Isophthalic acid bis-(4-fluoro-benzyl)-ester;~~  
~~Isophthalic acid bis-(3-fluoro-benzyl)-ester;~~  
~~Isophthalic acid bis-(4-methoxy-benzyl)-ester;~~  
~~Isophthalic acid bis-(3-methoxy-benzyl)-ester;~~  
~~Isophthalic acid bis-(1,3-benzodioxol-5-ylmethyl)-ester;~~  
~~N,N'-Bis-(3-fluoro-benzyl)-isophthalamide;~~  
~~4-Acetyl-isophthalic acid dibenzyl ester;~~  
~~4-Methoxycarbonylmethoxy-isophthalic acid dibenzyl ester;~~  
 N,N'-Bis-1,3-benzodioxol-5-ylmethyl-4-methoxy-isophthalamide;  
~~N-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N'-(4-methoxy-benzyl)-isophthalamide;~~  
~~4-Methoxy-N,N'-bis-(4-methoxy-benzyl)-isophthalamide;~~

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~~N-1,3-Benzodioxol-5-ylmethyl N'-(4-chloro-benzyl)-4-methoxy-~~  
~~isophthalamide;~~

~~N-Benzyl-4-methoxy-N'-(4-methoxy-benzyl)-isophthalamide;~~

~~N'-Benzyl-4-methoxy-N-(4-methoxy-benzyl)-isophthalamide;~~

~~4-Methoxy-N-(4-methoxy-benzyl)-N'-pyridin-4-ylmethyl-isophthalamide;~~

~~N'-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N-(2-phenoxy-ethyl)-~~  
~~isophthalamide;~~

~~N-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N'-(2-phenoxy-ethyl)-~~  
~~isophthalamide;~~

~~N-1,3-Benzodioxol-5-ylmethyl-N'-furan-2-ylmethyl-isophthalamide;~~

~~N'-1,3-Benzodioxol-5-ylmethyl-N-(2-ethoxy-ethyl)-4-methoxy-~~  
~~isophthalamide;~~

~~N,N'-Bis-(3-hydroxymethyl-phenyl)-isophthalamide;~~

~~N-Benzyl-4-methoxy-N'-(2-phenoxy-ethyl)-isophthalamide;~~

~~4-Methoxy-N,N'-bis-(4-methyl-benzyl)-isophthalamide;~~

~~4-Methoxy-N,N'-bis-(3-methoxy-benzyl)-isophthalamide;~~

~~N-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N'-(4-methoxy-benzyl)-~~  
~~isophthalamide;~~

~~N-1,3-Benzodioxol-5-ylmethyl-isophthalamide-acid;~~  
~~(4-carboxyphenyl)methyl-ester;~~

~~4-[[3-(3-Methoxy-benzylcarbamoyl)-benzoylamino]methyl]-benzoic~~  
~~acid;~~

~~4-Methoxy-isophthalic acid di-2,1,3-benzothiadiazol-5-ylmethyl ester;~~

~~4-[[3-(3-Methoxy-benzylcarbamoyl)-benzoylamino]methyl]-benzoic~~  
~~acid-methyl ester;~~

~~N-(3-Methoxy-benzyl)-N'-(4-nitro-benzyl)-isophthalamide;~~

~~N-(3,4-Dichloro-benzyl)-N'-pyridin-4-ylmethyl-isophthalamide;~~

~~N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-ethoxy-isophthalamide;~~

~~N-(4-Chloro-benzyl)-N'-(3-methoxy-benzyl)-isophthalamide;~~

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~~N-(3,4-Dichloro-benzyl)-N'-(3-methoxy-benzyl)-isophthalamide;~~  
~~N-(4-Methoxy-benzyl)-N'-(3-methoxy-benzyl)-isophthalamide;~~  
~~N,N'-Bis-(4-fluoro-3-methoxy-benzyl)-isophthalamide;~~  
~~4-Ethoxy-N1,N3-bis-(3-methoxy-benzyl)-isophthalamide;~~  
~~N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-ethoxy-isophthalamide;~~  
~~N-(3-Methoxy-benzyl)-N'-pyridin-3-ylmethyl-isophthalamide;~~  
~~N-(3-Methoxy-benzyl)-N'-pyridin-4-ylmethyl-isophthalamide;~~  
~~N1-1,3-Benzodioxol-5-ylmethyl-N3-pyridin-3-ylmethyl-isophthalamide;~~  
~~N-(3-Methoxy-benzyl)-N'-(3-trifluoromethoxy-benzyl)-isophthalamide;~~  
~~N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-isopropoxy-isophthalamide;~~  
~~4-Isopropoxy-N1,N3-bis-(3-methoxy-benzyl)-isophthalamide;~~  
~~N1-Benzyl-4-methoxy-N3-(4-methoxy-benzyl)-isophthalamide;~~  
~~N1-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N3-(4-methoxy-benzyl)-~~  
~~isophthalamide;~~  
~~N1-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N3-(2-phenoxy-ethyl)-~~  
~~isophthalamide;~~  
~~N1-Benzyl-4-methoxy-N3-(2-phenoxy-ethyl)-isophthalamide;~~  
~~N1-1,3-Benzodioxol-5-ylmethyl-N3-(4-chloro-benzyl)-4-methoxy-~~  
~~isophthalamide;~~  
~~N3-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N1-(4-methoxy-benzyl)-~~  
~~isophthalamide;~~  
~~N3-Benzyl-4-methoxy-N1-(4-methoxy-benzyl)-isophthalamide;~~  
~~N3-1,3-Benzodioxol-5-ylmethyl-4-methoxy-N1-(2-phenoxy-ethyl)-~~  
~~isophthalamide;~~  
~~N3-1,3-Benzodioxol-5-ylmethyl-N1-(2-ethoxy-ethyl)-4-methoxy-~~  
~~isophthalamide;~~  
~~4-Methoxy-N1-(4-methoxy-benzyl)-N3-pyridin-4-ylmethyl-~~  
~~isophthalamide;~~  
~~4-Amino-N1,N3-bis-1,3-benzodioxol-5-ylmethyl-isophthalamide;~~  
~~4-Acetylamino-N1,N3-bis-1,3-benzodioxol-5-ylmethyl-isophthalamide;~~

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~~N (3-Methoxy-benzyl)-N' pyridin-3-ylmethyl-isophthalamide;~~  
~~N (3-Methoxy-benzyl)-N' pyridin-4-ylmethyl-isophthalamide;~~  
~~N1,1,3-Benzodioxol-5-ylmethyl-N3-pyridin-3-ylmethyl-isophthalamide;~~  
~~N (4-Chloro-benzyl)-N' (3-methoxy-benzyl)-isophthalamide;~~  
~~N (3,4-Dichloro-benzyl)-N' (3-methoxy-benzyl)-isophthalamide;~~  
~~N (4-Methoxy-benzyl)-N' (3-methoxy-benzyl)-isophthalamide;~~  
~~N (3-Methoxy-benzyl)-N' (4-methyl-benzyl)-isophthalamide;~~  
~~N,N'-Bis (4-fluoro-3-methoxy-benzyl)-isophthalamide;~~  
~~((3-[(1,3-Benzodioxol-5-ylmethyl)-carbamoyl]-benzoyl)-benzyl-amino)-acetic acid;~~  
~~N-Benzo[1,3]dioxol-5-ylmethyl-isophthalamide(4-hydroxymethyl-benzoic acid)-ester;~~  
~~N (3,4-Dichloro-benzyl)-N' pyridin-4-ylmethyl-isophthalamide;~~  
~~N (3-Methoxy-benzyl)-N' (4-nitro-benzyl)-isophthalamide;~~  
~~4-[[3-(3-Methoxy-benzylcarbamoyl)-benzoylamino]-methyl]-benzoic acid-methyl ester;~~  
~~N-3-methoxybenzyl-isophthalamide(4-hydroxymethyl-benzoic acid)-ester;~~  
~~4-[[3-(3-Methoxy-benzylcarbamoyl)-benzoylamino]-methyl]-benzoic acid;~~  
~~N (3-Amino-benzyl)-N' (3-methoxy-benzyl)-isophthalamide;~~  
~~N (3-Methoxy-benzyl)-N' (3-nitro-benzyl)-isophthalamide;~~  
~~4-Ethoxy-N'1,N'3-bis (3-methoxy-benzyl)-isophthalamide;~~  
~~N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-ethoxy-isophthalamide;~~  
~~N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-propoxy-isophthalamide;~~  
~~N1,N3-Bis-1,3-benzodioxol-5-ylmethyl-4-isopropoxy-isophthalamide;~~  
~~N1,N3-Bis-2,1,3-benzothiadiazol-5-ylmethyl-4-methoxy-isophthalamide;~~  
 and  
 4-Methoxy-isophthalic acid di-2,1,3-benzothiadiazol-5-ylmethyl ester.

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**Claim 8 (original).** A pharmaceutical composition, comprising a compound of Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, diluent, or excipient.

**Claim 9 (original).** A pharmaceutical composition for inhibiting MMP-13 in a mammal, comprising an MMP-13 inhibiting amount of a compound of Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, diluent, or excipient.

**Claim 10 (amended).** A method for inhibiting MMP-13 in an animal, comprising administering to the animal an MMP-13 inhibiting amount of a compound of ~~Formula I~~ Claim 1, or a pharmaceutically acceptable salt thereof.

**Claims 11 and 12 (canceled).**

**Claim 13 (amended).** A method for treating breast carcinoma, comprising administering to a patient suffering from such a disease an anticancer effective amount of a compound of ~~Formula I~~ Claim 1, or a pharmaceutically acceptable salt thereof.

**Claim 14 (amended).** A method for treating a rheumatoid arthritis, comprising administering to a patient suffering from such a disease an effective amount of a compound of ~~Formula I~~ Claim 1, or a pharmaceutically acceptable salt thereof.

**Claim 15 (amended).** A method for treating a osteoarthritis, comprising administering to a patient suffering from such a disease an effective amount of a compound of ~~Formula I~~ Claim 1, or a pharmaceutically acceptable salt thereof.

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**Claim 16 (amended).** A method for treating a heart failure, comprising administering to a patient suffering from such a disease an effective amount of a compound of ~~Formula I~~ Claim 1, or a pharmaceutically acceptable salt thereof.

**Claim 17 (amended).** A method for treating a inflammation, comprising administering to a patient suffering from such a disease an effective amount of a compound of ~~Formula I~~ Claim 1, or a pharmaceutically acceptable salt thereof.